## REMARKS

### Status of Claims

Claims 1-20 were pending in this Office Action. By the present amendment, no claims are added or canceled. Accordingly, it is now claims 1-20, as amended, which are issue.

### The Office Action

In the Office Action mailed February 22, 2007, claims 1-20, all claims then pending, were rejected. Specifically, claims 1-13 were rejected under 35 U.S.C. §112, second paragraph, for particularly noted reasons.

Claims 15-17 and 20 were rejected under 35 U.S.C. §102(a), as being anticipated by the publication of Tsai (ACS 2002).

Claims 1-4 and 6-14 were rejected under 35 U.S.C. §103(a), as being obvious over prior patent 5,583,001 of Bobrow, in view of the publication of Lo et al. (JPR 2002). Claim 5 was rejected under 35 U.S.C. §103, as being obvious over the '001 patent of Bobrow and the publication of Lo, and further in view of the publication of Tsai.

Claims 18-19 were rejected under 35 U.S.C. §103(a), as being anticipated by the publication of Tsai, in view of the published patent application of Burton, US 2004/0235081.

In addition, claims 1-4 and 6-14 were rejected on the grounds of nonstatutory, obviousness-type double patenting over claims 1-24 of the Bobrow '001 patent, taken in view of the publication of Lo. Claim 5 was rejected on the grounds of nonstatutory, obviousness-type double patenting, as being unpatentable over the '001 patent of Bobrow, and the publication of Lo, as discussed above, and further in view of the publication of Tsai.

Applicant thanks the Examiner for the Office Action, and for the thorough explanation of the basis of the rejections.

## The Present Invention

Applicant will briefly recapitulate the principles of the present invention so as to point out significant distinctions between it and the prior art.

The present invention is directed to improvements in catalyzed reported deposition assays. As is described in the background section of this application, catalyzed reporter depositions are a class of amplified assays wherein the signal produced by interaction of a binding pair (antibodies, nucleic acids, haptens, and the like) is significantly amplified through the use of an analyte-dependent enzyme activation system (ADEAS). In the operation of this amplification system, an enzyme catalyzes a chemical reaction, and hence produces activation of, a conjugate which includes a substrate for the enzyme and a detectable label. This activated conjugate binds to, and localizes at a receptor site and the label associated therewith produces a detectable signal. Since this is a catalyzed reaction, a very small triggering event, namely the action of the binding pair, produces a very large resultant signal, thereby greatly amplifying the signal resultant from the binding event. As Applicant acknowledges, this basic mechanism has been adapted for use in an assay and is known in the art as represented by the Bobrow '001 patent where it is referred to as a CARD/ADEAS assay.

Applicant, who is the inventor of the prior art CARD/ADEAS assay, recognizes that significant improvements to the system, and advantages in sensitivity and control will be achieved if particular classes of conjugates incorporating substrates reactive with hydrolytic enzymes are employed in the system. As will be discussed in more detail hereinbelow, use of substrates reactive with hydrolytic enzymes, and in particular the specific classes of conjugates claimed herein, are nowhere shown or suggested in the prior art as being useable in, or having any advantages, in CARD/ADEAS detection systems.

**The Obviousness-Type Double Patenting Rejections**

Claims 1-4 and 6-14 were rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of the Bobrow '001 patent, taken in view of the Lo publication. In making this rejection, the Examiner is of the opinion that Bobrow '001 discloses a basic detection method utilizing an ADEAS system. The Examiner acknowledges that the Bobrow '001 patent "fails to disclose labeled conjugate comprising parahydroxy benzylic halide moiety as disclosed in claims 1 and 10." (Office Action at page 12, first paragraph).

However, while the Examiner concedes that the Bobrow '001 patent does not show the precise point of novelty of the present invention, it is the Examiner's position that the use of the specifically described and claimed conjugates incorporating hydrolytically reactive substrates, would be obvious in view of the teaching of Lo. In this regard, the Examiner refers to the fact that Lo describes the use of a compound having a structure which arguably falls within one of the generic structures set forth in claims 1 and 10. While Lo is directed to probes for labeling active enzymes, the Examiner holds that the incorporation of the compounds of Lo into a CARD/ADEAS assay would be obvious.

Applicant respectfully submits that in formulating this rejection, the Examiner is neglecting the explicit teaching of the Lo publication, which teaching specifically leads away from the claimed invention. Furthermore, Applicant respectfully submits that the benefits achieved through the use of the specific conjugates of the present invention are unanticipated, synergistic, and not at all to be expected from your review of the prior art of record.

The Lo publication teaches chemical compounds which are activity probes used to label active enzymes. They are not components of any type of catalyzed reporter deposition system.

The probes of Lo are used to detect enzyme activity in or from living cells. In this regard, see Lo, first page, left column, line 2:

> However, these genomic sequences provide only static information that does not describe the dynamic processes in living cells that mainly carried out by proteins. For example, the expression of genes in different tissues at different times is varied. It is thus important to locate and identify the protein products on a timely basis in order to understand their function.

In contrast, the present invention is operating on a completely different platform. As specifically recited in claim 1, the "activated conjugate binds to a site on a surface having a receptor for said activated conjugate, said receptor not being reactive with the analyte-dependent enzyme activation system . . ." Clearly, the system of the present invention is very different from that of Lo. There is no surface having any receptor in the publication of Lo. Therefore, given the very different mode and venue of operation of the chemistry of Lo, the Lo publication provides no teaching whatsoever which would suggest that any particular benefits would be achieved by the use of compounds which react with hydrolytic enzymes in Applicant's surface-binding chemistry detection system. Not only does the prior art not suggest advantages or desirability, or superior and unexpected results achievable through the use of such systems, in no way does it even begin to suggest that such chemistry could be incorporated into systems of the present invention. The sole teaching of Lo is of the existence of particular molecular compounds.

In claiming this invention, Applicant has specifically chosen to use a Jepson format so as to clearly identify the field of the present invention, namely CARD/ADEAS assays, and claims only that particular point of novelty of the present invention, namely the use of a very particular

and narrowly defined group of conjugates in CARD/ADEAS assays. Lo in no way shows or suggests this point of novelty or the unexpected results achieved therefrom.

Claim 5 was likewise subject to an obviousness-type double patenting rejection on the basis of the above described combination of Bobrow '001 and Lo, and further in view of the publication of Tsai. Claim 5 specifically recites that the Y group is a glycoside selected from the group consisting of galactose and glucose. The Examiner recognizes that the Bobrow '001 and Lo prior art does not show this element of the claims; but cites to the Tsai publication for its teaching of a compound comprising glucose connected through a beta glycoside linkage to a p-hydroxy benzylic fluoride moiety. On this basis, the Examiner holds that claim 5 is likewise obvious in view of the three cited references.

For the reasons discussed above, Applicant respectfully submits that this rejection is inappropriate because the Tsai publication discloses a system generally similar to that in the Lo publication (Lo is one of the authors of the Tsai publication). As such, the Tsai publication is also directed to compounds used to label active enzymes in living cells. Like Lo, Tsai does not show or suggest any system in which any activated conjugate covalently binds to a site on a surface having a receptor for the activated conjugate, as required by the claims at issue. For the reasons discussed above with regard to claims 1-4 and 6-14, the rejection of claim 5 is likewise inappropriate.

**The Rejections Under 35 U.S.C. §103**

Claims 1-14 are rejected under 35 U.S.C. §103(a), for reasons generally similar to those set forth with regard to the double patenting rejection, and for these same reasons, this rejection is inappropriate. Applicant will not restate all the arguments set forth above; but, does point out to the Examiner that the incorporation of the specifically claimed hydrolytically activatable

conjugates set forth in the claims at issue, provides unanticipated enhancements to the CARD/ADEAS assay system. This improvement is not an expected and anticipated improvement resultant from the substitution of a chemical system having one known functionality into a chemical system having another known functionality. The use of such conjugate in a CARD/ADEAS system where a catalyzed reporter molecules deposit onto a substrate is nowhere acknowledged or taught in the prior art and hence, the benefits of the combination are not at all anticipated.

Applicant points out that in making this particular rejection of the claims, the Examiner, at page 7, line 6 of the Office Action, states:

> Phosphatases (e.g. tyrosine phosphatase) present in the analyte remove phosphate group which leads to a reactive quinine methide intermediate that in turn alkylate nearby electron rich nucleophiles on the biocatalyst resulting in the biocatalyst being labeled, which can then be detected directly or indirectly.

This quotation makes clear that the Examiner is not fully appreciating the fundamental differences in the chemical systems of the present invention and that of the prior art. In the case of the prior art, the analyte (phosphatase) is the analyte-dependent enzyme activation system and is also the receptor. This is very different from the presently claimed invention. In order for the present invention to work, the activated conjugate needs to react with an immobilized receptor, separate from the analyte-dependent enzyme activation system. If one were to read the Lo (or Tsai) prior art, it is clear that it actually teaches away from any enablement of the present invention.

In view of all the foregoing, Applicant respectfully requests that the Examiner reconsider the rejection of these claims under 35 U.S.C. §103.

**The Bobrow '001 Patent Does not Qualify as Prior Art Under 35 U.S.C. §103(c)**

The foregoing rejections are further inappropriate since the Bobrow '001 patent is not prior art. The Bobrow '001 patent was, at the time that the present invention was made, owned by Perkinelmer LAS, the Assignee and owner of the present invention. As noted by the Examiner, in the Office Action, the Bobrow '001 patent was referenced for the rejection of this patent application under 35 U.S.C. §103(a). In accord with 35 U.S.C. §103(c), this rejection is improper, since both the Bobrow '001 patent and the present application were owned by Perkinelmer LAS at the time of the making of the present invention. The properties continue to be owned by Perkinelmer LAS.

The Bobrow '001 patent was originally filed in the name of E. I. du Pont de Nemours and Company, and was assigned to NEN Life Science Products, Inc. This Assignment is of record in United States Patent and Trademark Office at Reel 009178, Frame 0720, and following.

NEN Life Science Products merged into Perkinelmer Life Sciences, Inc. in January 2001, and Perkinelmer Life Sciences, Inc. subsequently changed its name to Perkinelmer LAS, Inc. on March 26, 2003. Therefore, the Bobrow '001 patent was owned by the owner of the present application, at the time the invention was made. Documents evidencing the merger and name change are attached hereto as Appendix A.

In view of all of the foregoing, the Bobrow '001 patent is not citable as prior art.

**In View of the Present Amendment, Claims 15-20 are Allowable**

Claims 15-17 and 20 were rejected under 35 U.S.C. §102(a), as being anticipated by the publication of Tsai. In addition, claims 18 and 19 were rejected as being obvious over the combination of the Tsai publication taken in view of U.S. patent application No. 2004/0235081 of Burton.

In formulating these rejections, the Examiner points to particular structures in Tsai which are asserted to fall under the second generic formula in independent claim 15. The Examiner acknowledges that those compounds of Tsai are not esters, and hence do not anticipate claims 18 and 19; but, the Examiner is holding that the use of esters in compounds of the type shown in Tsai would be obvious in view of the teaching of Burton.

By the present amendment, Applicant has narrowed claim 15 to exclude the second generic structure. The first generic structure is not shown or suggested in the prior art, and hence, claims 15-20 now overcome all rejections under 35 U.S.C. §102 and §103.

**The Amended Claims Overcome the Rejections Under 35 U.S.C. §112, First Paragraph**

Claims 1-13 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In particular, independent claims 1 and 10 were held to be unclear with regard to language characterizing the various reacting species in the CARD/ADEAS system.

By way of background, Applicant respectfully submits that CARD/ADEAS assay systems, and chemistries for their implementation, are well known in the art. The present invention is directed to a particular improvement in such systems resultant from the use of a particular group of conjugated enzyme substrates in such systems.

The operation of such CARD/ADEAS is extensively described in the prior art, including the prior art cited and incorporated by reference in the present application. For example, U.S. Patent 6,399,299 includes a very good and detailed description of the operational of a CARD/ADEAS analytical system, and this disclosure is found at column 3 and column 4. As it is known and detailed in the prior art, in assays of this type, a reaction between appropriate species forms a specific binding pair. This pair can be an antibody/antigen, nucleic acid pair, or any other such binding pair. This binding pair is immobilized at a particular location on a solid

support, and this is typically accomplished by previously affixing one member of the binding pair to the support so that when a solution containing an analyte which is the other member of the binding pair, is contacted with the solid support, the analyte binds to its appropriate counterpart and is immobilized on the support. In these analytical systems, an enzyme is also immobilized on the support along with the specific binding pair. As detailed in the prior art, this can be accomplished by either first coupling the enzyme to the free species in the analyte prior to formation of the pair, or by subsequently coupling the enzyme to a member of the pair by various detailed processes. In any event, the result of this step of the process is that at every location where a specific binding pair is immobilized on the support, the activated conjugate, and its label, are also immobilized proximate thereto. Because of the catalytic effect of the enzyme, a single binding pair can result in the immobilization of a number of labeling species proximate thereto. In this manner, amplification of the resultant signal is achieved.

Applicant apologizes to the Examiner for any lack of clarity in the originally presented claims. By this amendment, Applicant has rewritten independent claims 1 and 10 to more fully describe the sequence of reactions in the CARD/ADEAS assay. As mentioned above, all of this description constitutes background material and is well known in the art and fully supported in the present application. The basic CARD/ADEAS process is known to those of skill in the art and the novelty of the invention resides in the use of a particular labeled conjugate in the process.

In view of the foregoing, Applicant respectfully submits that all objections under 35 U.S.C. §112, second paragraph, are overcome.

## Conclusion

By the present amendment, all rejections and objections are overcome. The application is in condition for allowance. Any questions, comments or suggestions the Examiner may have should be directed to the undersigned attorney.

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Respectfully submitted,

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